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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/626,761	07/24/2003	James P. Elia	1000-10-C3	1741

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EXAMINER	
KEMMERER, ELIZABETH	
ART UNIT	PAPER NUMBER
1646	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/626,761	ELIA, JAMES P.	
	Examiner	Art Unit	
	Elizabeth C. Kemmerer, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

The response of 08 February 2007 has been entered.

Claims 1-33 are canceled. Claims 34-44 are under examination.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34-44 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this new matter rejection is originally set forth at pp. 2-3 of the previous Office Action (mailed 22 September 2006).

Applicant's arguments (pp. 3-4, Response received 08 February 2007) have been fully considered but are not found to be persuasive for the following reasons.

At the second paragraph of p. 3 of the remarks, Applicant points to several places in the specification and argues that these citations refer to both generic and specific disclosures including the treatment of organs to improve function and the formation of an artery. Applicant reasons that it is apparent that such generic and specific disclosure is pertinent to the enablement of the claimed invention and thus must

be read and evaluated by the examiner. This has been fully considered but is not found to be persuasive. Applicant is assured that the examiner has indeed read the entire disclosure. However, the passages referred to by Applicant do not support the instant claims' limitations, namely, inserting stem cells or germinal cells into a pancreas, growing Islets of Langerhans, and restoring insulin production. These phrases do not appear in the specification, nor do they flow naturally therefrom.

Applicant points to p. 47, lines 7-21 and p. 52, lines 7-11 as providing written description for the claimed invention. These two sections have been carefully reviewed and also are not found to provide written description for the limitations in the instant claims. Neither are directed to inserting stem cells or germinal cells into a pancreas, growing Islets of Langerhans, and restoring insulin production.

Applicant argues that the examiner failed to consider the entire disclosure and erroneously restricted the factual determination to the elected species. Citing In re Anderson and In re Johnson and Farnham (citations in Applicant's remarks), Applicant urges that the entire disclosure must be considered. Applicant points to p. 3 of the Office Action as evidencing the allegedly flawed reading of the specification. This has been fully considered but is not found to be persuasive. Again, Applicant is assured that the entire disclosure was read and considered. The instant claims recite the following limitations: inserting stem cells or germinal cells into a pancreas, growing Islets of Langerhans, and restoring insulin production. These limitations are not found in the specification as originally filed.

Claims 34-44 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The basis for this rejection is originally set forth at pp. 3-5 of the previous Office Action (mailed 22 September 2006).

Applicant's arguments (pp. 4-11, Response received 08 February 2007) have been fully considered but are not found to be persuasive for the following reasons.

Applicant argues that the generic disclosure supports enablement of the claims. Applicant urges that the scope of the present invention is within the scope of the disclosure. Applicant argues that the disclosure must be considered in its entirety rather than the allegedly incorrect manner in which it was done. This has been fully considered but is not found to be persuasive. Again, Applicant is assured that the entire disclosure has been considered. The specification broadly asserts that the administration of cells can achieve diverse effects, including growth of any "hard" tissue or "soft" tissue (p. 20), formation of entire new organs (p. 32) or portions of organs (p. 46), restoration of function in any organ (p. 47), formation of auxiliary organs (p. 49), correction of necrosis (p. 49), replacement of missing limbs or body parts (p. 50), treatment of inflammation (p. 50), correction of musculoskeletal injuries or deficiencies (p. 50), formation of hybrid organs (p. 50), etc. No guidance or details are provided as to *how* to achieve these remarkable effects, most of which have never been achieved in this art to this day. After review of the entire disclosure, it was found that there was very

little support or guidance regarding achieving the effects recited in the instant claims. The courts have stated that "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable". Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 (1997). The courts have also stated that "[t]ossing out the mere germ of an idea does not constitute an enabling disclosure... [R]easonable detail must be provided in order to enable members of the public to understand and carry out the invention" (Genentech Inc. v. Novo Nordisk A/S, supra).

Applicant urges that the disclosed administration techniques were well established in the medical arts prior to the invention and must be considered in any reasonable evaluation of enablement. Applicant also asserts that stem cells were well known and available. Applicant characterizes Dr. Elia's contribution to the medical arts was that growth of new arteries effect organ repair, including heart and brain, could be accomplished through new use of old administration techniques and old growth factors, including cellular materials. Applicant concludes that only routine experimentation would be required for one skilled in the art to make and use the claimed invention. This has been fully considered but is not found to be persuasive. The specification does not disclose *how* to use cells to achieve growth of arteries and effect organ repair. Furthermore, the claims also require growing Islets of Langerhans in the pancreas. Again, the specification does not disclose *how* to achieve this result. Finally, there is evidence in the art that others have not achieved the desired results while using the "old" administration methods and cellular materials. Specifically, Lechner et al. failed to

see transdifferentiation into pancreatic beta cells after transplantation of bone-marrow cells into mice (Diabetes 2004; 53: 616-23). Rajagopal et al. failed to derive beta cells from embryonic stem cells (Science 2003; 299: 363). Finally, Hussain et al. (2004, Lancet 364:203-205) state, "...early reports seem confusing and conflicting. Embryonic and adult stem cells are potential sources for beta-cell replacement and merit further scientific investigation. Discrepancies between different results need to be reconciled. Fundamental processes in determining the differentiation pathways of stem cells remain to be elucidated, so that rigorous and reliable differentiation protocols can be established." Thus, it is clear that the state of the art in this approach to restoration of islet cells and function in pancreas was still considered complex and unpredictable even in 2004, after Applicant's filing date.

Applicant argues that the examiner has ignored the high level of skill in the art, which is alleged to be "especially egregious" when it is considered that the administration techniques and materials are well known in the art. This has been fully considered but is not found to be persuasive. Admittedly, the level of skill in the art was high at the time of the invention. However, it is clear from the reports in the literature that those skilled in this art were unable to achieve the required results in the claims even after the filing date. See Lechner et al., Rajagopal et al., and Hussain et al., cited in the previous Office Action and reviewed above. Thus, the high level of skill in the art was clearly not sufficient to make up for the lack of other factors deemed important for enablement, including the quantity of experimentation required, the lack of detailed

guidance in the disclosure, the absence of working examples, the complex and unpredictable nature of the invention, and the contradictory reports in the art.

Applicant characterizes the examiner's treatment of the remaining seven Wands factors as cursory and mere speculation. Applicant urges that such cannot be accorded evidential weight. This has been fully considered but is not found to be persuasive because it is factually incorrect. The absence of working examples is factual based on the evidence of the specification. The complexity and unpredictability on the art, as well as the state of the art being contradictory, are findings based upon the evidence brought forth in Lechner et al., Rajagopal et al., and Hussain et al. The large quantity of experimentation required is also evidenced by the lack of detailed guidance in the specification regarding how to achieve the required results, as well as the amount of detail reported in the materials and methods sections of relevant art, such as Lechner et al. Finally, the large breadth of the claims is evidenced by the wording of the claims themselves.

Applicant takes issue with Hussain et al., characterizing it as irrelevant since it deals with rodents rather than humans. Applicant points to Fernandez et al. (2005, reference AV in the IDS received 14 June 2006) as more relevant as it is directed to a human study. This has been fully considered but is not found to be persuasive. Numerous publications are of record that use rodent models for stem cell transplantation studies and for diabetes therapies. These have been cited both by the examiner and by Applicant. The mere existence of these publications indicate that those skilled in the art accept rodents as an acceptable model for this purpose. No

evidence has been brought forth that those skilled in the art do not see rodents as acceptable models for this disease in humans. Furthermore, Hussain et al. clearly addresses issues in humans. See, for example, p. 203, paragraph bridging 1st and 2nd columns; p. 203, 2nd paragraph of 2nd column; p, 204, last full paragraph of 2nd column; etc. Regarding Fernandez et al., this evidence is not commensurate in scope with the claims. Fernandez et al. used a specific type of cell ($752x10^6$ ($\pm$ 445), CD34(+)$7.8x10^6$ ($\pm$ 5.45 and CD34(+)CD38(-)=$1.02x10^6$($\pm$0.82) autologous bone marrow mononuclear cells) which is not recited in the claims nor disclosed in the specification. Fernandez et al. administered the cells through the spleen artery with occlusion of the distal lumen to derivate the cells to the pancreas' tail. This administration method is not recited in the claims nor disclosed in the specification. In fact, Fernandez et al. serve as evidence of the type of specific guidance and further act of invention that would have been required before the skilled artisan could achieve the results required in the claims. For example, there is post-filing date evidence that not all bone marrow stem cells are appropriate, contradicting the claims and instant specification. For example, Yamaoka (2003, Expert Opin. Biol. Ther. 3(3):425-233) reports that mesenchymal stem cells derived from bone marrow do not differentiate into pancreatic cells that produce insulin. See p. 425, Abstract; p. 430, top of left column.

Applicant advises the examiner that the Court decided against the USPTO on the enablement issue in Wands. Applicant argues that the fact pattern in the instant application is similar to that of Wands. This has been fully considered but is not found to be persuasive. The examiner is aware of the findings in Wands. The instant fact

pattern differs substantially from that in Wands, however, especially with regard to the detailed guidance and working examples provided in the Wands application, which are missing in the instant application. Furthermore, the nature of the invention and the state of the prior art are completely different in Wands when compared to the instant application. The instant fact pattern is more similar to that found in Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 (1997), wherein the courts have stated that "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable". The courts have also stated that "[t]ossing out the mere germ of an idea does not constitute an enabling disclosure... [R]easonable detail must be provided in order to enable members of the public to understand and carry out the invention" (Genentech Inc. v. Novo Nordisk A/S, supra).

Finally, Applicant cites In re Neave and states that the examiner's opinion is of little weight. This has been fully considered but is not found to be persuasive. The instant rejection is maintained upon a careful, fresh consideration of the totality of the evidence. The evidence includes the specification as well as the art cited by Applicant and the art cited by the examiner. The preponderance of the totality of the evidence supports the rejection, as discussed in detail above.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number is (571) 272-0874. The examiner can normally be reached on Monday through Thursday, 7:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D. can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Elizabeth C. Kemmerer

ECK

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PRIMARY EXAMINER